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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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07/13/2006

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EXAMINER

LUM, LEON YUN BON

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1641

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/585,985	Applicant(s) KOHNO ET AL.	
	Examiner Leon Y. Lum	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 12-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 12, 2010 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishibu *et al.*, Analytical Biochemistry (2003) 319:88-95 ("Nishibu").

i. Independent claim 1 is anticipated

Nishibu teaches a method of blotting proteins onto a polyvinylidene difluoride (PVDF) membrane, comprising the steps of (1) mixing a protein solution with ethanol, TCA and SDS to produce a sample and (2) placing the sample in a vacuum pump

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attached to a PVDF membrane, thereby allowing the protein to become immobilized onto the membrane. See page 89, left column second paragraph spanning to the right column, second paragraph. Since Nishibu teaches ethanol, TCA and SDS, the reference teaches the claimed "lower alcohol, and a halogenocarboxylic acid and/or a long chain alkyl sulfate," as claimed. Moreover, the PVDF membrane teaches the claimed "solid-phase having hydrophobic surface." Accordingly, Nishibu teaches all of the claimed elements presented in claim 1.

ii. Dependent claims 2-11 are anticipated

Claims 2-11 are dependent on claim 1 and anticipated by Nishibu for the following reasons.

Regarding claims 2-5, Nishibu teaches ethanol, TCA and SDS. See *supra* rejection of claim 1.

Regarding claims 6-8 and 10-11, Nishibu teaches that the blotting solution can contain 2-5% TCA, 30-50% ethanol and 0.1-0.4% SDS. See page 89, right column, second paragraph. Accordingly, claims 6-8 and 10-11 are anticipated for all of the foregoing reasons, including the reason directed at base claim 1 above.

Regarding claim 9, Nishibu teaches that the proteins are blotted onto PVDF. See *supra* rejection of claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley *et al.*, Biotechniques (1991) 10(6):731-732 ("Cheley"), cited in the IDS filed

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July 22, 2008, in view of Jacobson, *Electrophoresis* (1990) 11:46-52, cited in the IDS filed July 13, 2006.

i. Independent claim 1 is obvious

Cheley describes a method of immobilizing protein samples to a nitrocellulose membrane using a dot blotter, in which the samples are mixed with a solution of SDS and TCA. See page 731 (right column, third paragraph). The skilled artisan would recognize that SDS and TCA are, respectively, species of a halogenocarboxylic acid and a long chain alkyl sulfate. Accordingly, Cheley teaches "contacting the protein with the solid-phase" in the presence of "a halogenocarboxylic acid" and "a long chain alkyl sulfate," as claimed. Moreover, because the proteins are being blotted onto a nitrocellulose membrane, they are being selectively transferred onto the membrane from a different source. *Id.* Accordingly, the proteins are considered to be "filtered." This interpretation is supported by the ordinary and plain meaning of the term "filter," which is defined as "remove by means of a filter." Merriam-Webster OnLine, available at <http://www.merriam-webster.com/dictionary/filter>[2] (last accessed on July 3, 2009). Here, the proteins are being removed by the nitrocellulose membrane after being mixed with numerous reagents, albeit immobilized on the membrane, see page 732, with the reagents presumably passing through the membrane. The specification does not contradict this interpretation because, as indicated in the new matter rejection above, a filtering step is neither described nor suggested. Accordingly, Cheley teaches the claimed "filtering" step.

Although Cheley teaches a solid-phase, the reference does not teach that the solid-phase has a hydrophobic surface. Cheley also does not teach that a lower alcohol is included with the halogenocarboxylic acid and long chain alkyl sulfate.

Jacobson describes an electrophoretic transfer method that uses a transfer buffer comprising methanol and SDS to transfer proteins from a gel to various types of membranes. See page 47 (left column, first paragraph). The membranes include nitrocellulose, nylon and PVDF. *Id.* (right column, third paragraph). Methanol is a well-known lower alcohol and PVDF is a well-known hydrophobic material, as evidenced by Applicants' specification on pages 9-10, paragraph 0022; and page 11, paragraph 0029. Although Jacobson teaches that the PDVF membrane does not provide the most effective protein binding out of all the membranes tested, the PVDF membrane provides high mechanical strength, which is an advantage when colloidal gold and India Ink are used for staining the proteins. See page 50 (right column, first paragraph). Moreover, Jacobson teaches that methanol improves protein binding efficiency. See page 47 (right column, second paragraph); page 49 (right column).

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Cheley's method to include a PVDF membrane and methanol in the transfer buffer. The skilled artisan would have been motivated to perform the modification based on Jacobson's teaching that a PDVF membrane provides high mechanical strength for specific labeling techniques and methanol increases the likelihood of protein binding. Although Jacobson describes methanol's effectiveness in terms of nitrocellulose, the skilled artisan would have found it obvious to apply methanol

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to the PVDF membrane. Indeed, since PVDF does not provide as effective a binding efficiency as the other membranes tested, the skilled artisan would have attempted to use methanol on PVDF, given it's penchant for improving protein binding on other membrane materials.

ii. Dependent claims 2-5 and 8-10 are obvious

Claims 2-5 and 8-10 are dependent on claim 1 and obvious over the prior art for the following reasons.

Regarding claims 2-5 and 10, Cheley teaches TCA and SDS and Jacobson teaches methanol. *See supra* rejection of claim 1.

Regarding claim 8, Jacobson teaches that the SDS is in a concentration of 0.1%. *See page 47* (left column first paragraph).

Regarding claim 9, Jacobson teaches that the membrane is PVDF. *See supra* rejection of claim 1.

Claims 6-7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson, as applied to claim 1.

Regarding claim 11, Jacobson teaches that the SDS is in a concentration of 0.1% and that the membrane is PDVF. *See page 47* (left column first paragraph and right column, third paragraph).

Cheley and Jacobson, however, do not teach the specifically claimed percentages directed to methanol (claims 6 and 11) and halogenocarboxylic acid (claims 7 and 11).

With the foregoing description, one of ordinary skill in the art would have found it obvious to modify Cheley's TCA and Jacobson's methanol by optimizing the percentages of these compounds to arrive at the claimed ranges. The optimization principle is supported by the *Aller* case, which held that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955); see also MPEP 2144.05. In *Aller*, the claimed process recited a range of temperatures and a range of acid concentrations. *Id.* The court held the process obvious over a reference process that recited the same steps as claimed, but a temperature and acid concentration outside the claimed range. *Id.* Here, the general conditions of the transfer buffer are taught by Cheley and Jacobson, together describing methanol and TCA and thereby teaching the claimed "lower alcohol" and "halogenocarboxylic acid." Although methanol and TCA are described as being in a percentage outside of the claimed percentage ranges, the skilled artisan, following *Aller* and using routine experimentation, would have found it obvious to modify the percentages disclosed in Cheley and Jacobson to arrive at the claimed ranges.

Response to Arguments

I. Rejection of claims 1-11 under 35 U.S.C. 102(b)

Applicants submitted a certified English translation of PCT/JP2004/000504 and opine that this submission perfects priority to the '504 application and overcomes the

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Nishibu reference. See Response filed February 12, 2010. For the following reason, however, Nishibu is still a valid reference under 35 U.S.C. 102(b).

Under 35 U.S.C. 365(b), an international application designating the United States shall be entitled to the right of priority based on a prior international application designating at least one country other than the United States. See *a/so* MPEP 201.13(b). However, foreign priority has restrictions. Germane to the instant case is the fact that the statutory bar under 35 U.S.C. 102(b) stems from the date of U.S. filing, not the foreign filing date. See MPEP § 201.13(III) (stating that “the 1 year bar of 35 U.S.C. 102(b) dates from the U.S. filing date and not from the foreign filing date”); see *a/so* MPEP 201.13(b) (stating that “[t]he formal requirements for obtaining the right of priority under 35 U.S.C. 365 differ somewhat from those imposed by 35 U.S.C. 119(a)-d() and (f), although the 1-year bar of 35 U.S.C. 102(b), as required by the last clause of section 119(a) is the same”) (emphasis added).

Here, the instant application is a national stage application of PCT/JP05/00737, filed January 21, 2005, and claims priority to PCT/JP2004/000504, filed January 21, 2004. The ‘504 PCT application designates at least one country other than the United States; hence, it falls under section 365(b) and the instant application is therefore granted foreign priority to January 21, 2004. However, because this is a foreign filing date, the U.S. filing date is January 21, 2005 for purposes of section 102(b). And because the Nishibu reference was published in 2003, it qualifies as a 102(b) reference against the instant claims.

Consequently, Applicants' English translation does not overcome the fact that the instant application is barred by the Nishibu reference under 35 U.S.C. 102(b).

II. Rejection of claims 1-5 and 8-10 under 35 U.S.C. 103(a)

Applicants traverse the rejection of claims 1-5 and 8-10 under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson based on two arguments. See Response filed October 7, 2009. These arguments are not convincing for the following reasons.

Applicants argue that because Jacobson indicates that SDS is not preferable for binding in nitrocellulose, the skilled artisan would not have motivation to modify Cheley's method with Jacobson. See pages 3-5. Jacobson, however, is relied upon in part to teach a PVDF membrane, not nitrocellulose. The combination of Cheley and Jacobson would therefore have PVDF, not nitrocellulose, as the immobilizing membrane. Although PVDF and nitrocellulose are equivalent materials for the same function, Jacobson does not indicate that PVDF in the presence of SDS would cause a decrease in binding like nitrocellulose does. Indeed, based on Jacobson, the skilled artisan would not have recognized that SDS's effect on protein binding to nitrocellulose would translate into the same type of binding in PVDF. Moreover, Jacobson describes PVDF as a membrane with good mechanical strength and that using methanol would increase binding. See *supra* rejection of claim 1. Accordingly, even if SDS did reduce binding with a PVDF membrane, for which there is no evidence in the record to show this would occur, the methanol would provide a counter to this decrease and PVDF's mechanical

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qualities provide an incentive for using it as a protein substrate. One of ordinary skill in the art would therefore still have a reason to combine Jacobson with Cheley's method.

Applicants also argue that the instant invention allows immobilization of proteins in the presence of SDS, which is unexpected. See pages 6-7. Applicants specifically point to Table 3 of the specification as proof of this unexpected result. However, Table 3 compares the instant invention to a liquid-phase method using Pyromolex solution. See paragraph 0204 of the pre-grant publication. Because neither Cheley nor Jacobson use Pyromolex, Applicants' explanation of unexpected results is not convincing.

The rejection of claims 1-5 and 8-10 is therefore maintained.

III. Rejection of claims 6-7 and 11 under 35 U.S.C. 103(a)

Applicants traverse the rejection of claims 6-7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson. See page 7. Applicants traversed this rejection insofar as the rejection against base claim 1. But because Applicants' arguments are not convincing, *see supra* previous section, they do not overcome the rejection against the instant claims.

The rejection of claims 6-7 and 11 is therefore maintained.

Conclusion

No claims are allowed.

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All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Unsu Jung/
Primary Examiner, Art Unit 1641